



PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT Article 36 and Rule 70)

| | | | |
|---|---|---|--|
| Applicant's or agent's file reference 03/103 PCT | | FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416) | |
| International application No. PCT/EP 03/03984 | International filing date (day/month/year) 16.04.2003 | Priority date (day/month/year) 16.04.2002 | |
| International Patent Classification (IPC) or both national classification and IPC C12Q1/70 | | | |
| Applicant DOT DIAGNOSTICS B.V. et al. | | | |
| <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 1 sheets.</p> | | | |
| <p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the opinion</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Rule 68.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p> | | | |
| Date of submission of the demand 17.11.2003 | | Date of completion of this report 20.07.2004 | |
| Name and mailing address of the International preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 | | Authorized Officer Barz, W Telephone No. +49 89 2399-7320  | |

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03/03984**

I. Basis of the report

1. With regard to the elements of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-16 as originally filed

Claims, Numbers

1-5 received on 14.04.2004 with letter of 09.04.2004

Drawings, Sheets

1/3-3/3 as originally filed

Sequence listing part of the description, pages:

1-18, as originally filed

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
☒ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03/03984**

5. ☐ This report has been established as if (some of) the amendments had not been made; since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|-----|
| Novelty (N) | Yes: Claims | 1-3 |
| | No: Claims | 4-5 |
| Inventive step (IS) | Yes: Claims | 1-3 |
| | No: Claims | 4-5 |
| Industrial applicability (IA) | Yes: Claims | 1-5 |
| | No: Claims | |

2. Citations and explanations

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP03/03984

ITEM I:

The amendments to **claims 1** (replacement of the expression "microarrays with various HPV specific capture probes" by the expression "microarrays with various HPV specific capture probes in the 3' end of the E1 region") and to **claim 4** (replacement of the expression "solid supports containing HPV capture probes" by the expression "solid supports containing capture probes in the 3' end of the E1 HPV region") (underlinings added) have been disregarded for the establishment of this report (Rule 70.2 © PCT), because the original application (including the passages cited in the Applicant's letter dated 09.04.04) discloses neither microarrays nor other solid supports containing such capture probes. Concerning the Applicant's reference to Table 1 of the present application, it has to be pointed out that even if the primer sequences in that table are indeed selected from the 3' end of the HPV E1 region (which is, however, not apparent from the present application), such list of primer sequences would not justify a generalization such a "HPV specific capture probes in the 3' end of the E1 region". Consequently, the amendment is considered to go beyond the disclosure as filed, in contrast to the requirements of Article 34.2 (b) PCT.

ITEM V:

Reference is made to the following documents D1-D3:

- D1: WO 01 68915 A (PARK T.-S. ET AL.), 20 September 2001;
- D2: WO 02 26377 A (BECKMAN COULTER INC), 4 April 2002;
- D3: WO 02 02794 A (CAPITAL BIOCHIP COMPANY LTD), 10 January 2002;

1. NOVELTY

Claims 4-5 do not meet the requirements of Article 33(2) PCT for the following reasons:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP03/03984

Due to the broadness of present **claims 4-5**, the subject-matter of said claims is not novel in the sense of Article 33(2) PCT, because kits comprising a "device suitable for carrying out the detection method [...] of claims 1-3" and "a number of primer sets" as well as the additional features of said claims are disclosed in documents D1 (abstract; examples 1-4; claim 1), D2 (abstract; claim 1), and D3 (abstract; claims 1 and 22). It is noted that primers for the amplification of the HPV E1 gene are not a feature of present claims 4-5.

2. INVENTIVE STEP

Upon reconsideration, the International Preliminary Examining Authority is of the opinion that **claims 1-3** of the present application appear to meet the requirements of Article 33(3) PCT for the following reasons:

- 2.1 Document D1, which is considered to represent the closest prior art, discloses a detection method for HPV using a microarray with various HPV-specific capture probes (abstract; examples 1-4; claim 1). Compared to said prior art detection method, the subject-matter of present **claim 1** differs in that the E1 gene of HPV is amplified and labelled (whereas E1 is not explicitly mentioned in D1). Therefore, the technical problem to be solved by said claim is the provision of an alternative HPV detection method.

The subject-matter of present **claim 1** can be acknowledged as involving an inventive step (Article 33(3) PCT), because the use of capture probes specific for the HPV E1 gene is not obvious for the following reason: As convincingly shown in the present description (page 6, line 15 to page 7, line 2), primers can be selected from the HPV E1 gene which allow subdivision of all HPV types into clusters, thereby allowing the assignment of previously unassigned HPV types either as low or high risk mucosal types of HPV. In other words, due to the greater diversity in the HPV E1 region between the various HPV types, less obvious consensus primer can be defined in this region which results in greater reliability of the hybridization step and thereby in the HPV typing.

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP03/03984

- 2.2 The dependent **claims 2-3** are dependent on claim 1 and therefore also meet the requirements of the PCT with respect to inventive step (Article 33(3) PCT).

3. INDUSTRIAL APPLICABILITY

The subject-matter of **claims 1-5** appears to be industrially applicable in the sense of Article 33(4) PCT.

4. FURTHER COMMENTS

- 4.1 **Claim 4** is unclear (Article 6 PCT), because the primer sets described in part b) of said claim are not defined concerning their sequence (binding to which target sequences?). Therefore, the reader is unable to know which primer sets are comprised in the kit of claim 4.
- 4.2 The expression "A kit comprising according to claim 4" (underlining added) used in present **claim 5** is grammatically unclear (Article 6 PCT).